

What Is Claimed Is:

1. 1. An *in vivo* method for identifying a diabetes-mediating protein, comprising:

- (a) obtaining cells or tissue which secrete insulin or are capable of developing into insulin-secreting cells;
- (b) transplanting said cells or tissue into a host mammal, wherein said host mammal is at risk for development of diabetes;
- (c) removing said transplanted cells or tissue from said host mammals at a plurality of time periods between transplantation and development of diabetes;
- (d) analyzing the protein expression of said removed cells or tissue,
- (e) comparing the expression of said protein at one time period in the presence of diabetes development with the expression of said protein in the absence of diabetes development to identify a protein which exhibit an altered expression as a result of development of diabetes, wherein said protein is a diabetes-mediating protein.

2. The method of claim 1, wherein said cell is a pancreatic islet cell or a β cell.

3. The method of claim 1, wherein said host mammal is immunologically compatible with said transplanted cell.

4. The method of claim 1, wherein said analysis of protein expression is by gel electrophoresis, immunoblotting, mass spectrometry, or chromatography.

5. The method of claim 4, wherein said electrophoresis is two dimensional gel electrophoresis.

6. An isolated diabetes-mediating protein identified through the process of claim 1.

7. A diabetes-mediating protein, wherein said protein is characterized as exhibiting an altered expression during development of diabetes, relative to expression of the same protein in the absence of diabetes.

8. The diabetes-mediating protein of claim 7, wherein said protein is selected from the group consisting of the proteins listed in Tables 1 and 2.

9. The diabetes-mediating protein of claim 7, wherein said protein is selected from the group of proteins characterized as having the mass spectroscopic characteristics of a protein shown in FIGs. 6-48.

10. The protein of claim 7, wherein said protein is a protective protein, characterized as a protein capable of:

- (a) protecting against the development of diabetes in a subject at risk for the development of diabetes;
- (b) delaying the onset of diabetes in a subject at risk for the development of diabetes;

5 or

- (c) ameliorating the symptoms of diabetes in a subject at risk for development of

diabetes.

11. The protein of claim 7, wherein said protein is a deleterious protein, characterized as a protein capable of:

- (a) enhancing the development of diabetes;
- (b) increasing the risk of a subject developing diabetes;
- (c) reducing the time required for development of diabetes in a subject at risk for development of diabetes; or
- (d) increasing the severity of the symptoms of diabetes.

12. A method for predicting the development of diabetes, comprising:

- (a) measuring the expression of one or more of a protein shown in Table 1 in a sample obtained from a test subject;
- (b) measuring the expression of one or more of a protein shown in Table 2 in a sample obtained from a test subject; and
- (c) comparing the expression of the proteins of steps (a) and (b) relative to expression in a control sample;

wherein changes in a one or more of the proteins of Tables 1 and 2 is indicative of the development of diabetes.

13. The method of claim 12, wherein said sample is any one of a cell, cells, or tissue expressing one or more of the diabetes-mediating proteins listed in Tables 1 and 2.

14. An *in vitro* method of identifying a protective or deleterious diabetes-mediating protein, said method comprising:

- (a) transfecting a cell with a polynucleotide encoding a diabetes-mediating protein under conditions in which the polynucleotide is expressed as a protein; and
- (b) determining the effect of said expressed protein on said cell, wherein said effect is measured as a change in one or more cell functions in the absence or presence of a cytokine, wherein said cell functions are one or more of nitrous oxide (NO) production, insulin secretion, cell survival, protein expression, and cytotoxicity.

15. An *in vivo* method of identifying a protective or deleterious diabetes-mediating protein, said method comprising:

- 5 (a) generating a transgenic mammal expressing a diabetes-mediating protein under conditions in which said protein is expressed; and
- 10 (b) determining the effect of said protein expression on the development and timing of diabetes onset, wherein a protective protein is one which prevents, inhibits, or slows the development of diabetes in a subject at risk for diabetes, and a deleterious protein is one that causes development of diabetes, increases the risk of development of diabetes, increases the severity, or decreases the period of time required for the development of diabetes in a subject at risk for developing diabetes.

15 16. A transgenic non-human mammal comprising an exogenous diabetes-mediating protein transgene.

17. A assay method for screening compounds, wherein said compounds are capable of effecting the expression of a diabetes-mediating protein, comprising:

- 20 (a) administering a test compound to the transgenic mammal of claim 16;
- (b) measuring the effect of said compound on the incidence and timing of the development of diabetes, wherein said compound inhibits, decreases, induces, or increases the expression of said protein.

25 18. A compound identified by the assay method of claim 17, characterized as:

- 30 (a) inducing or enhancing the expression of an endogenous protective protein; or
- (b) suppressing or inhibiting the expression of a deleterious diabetes-mediating protein; wherein the compound is capable of delaying or preventing the development of diabetes in a subject at risk for development of diabetes.

35 19. A method of treating or preventing diabetes or a diabetes-related disorder, comprising administering a compound capable of preventing or delaying the development of diabetes in a subject at risk for development of diabetes, or capable of ameliorating the symptoms of diabetes in a diabetic subject.

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20. The method of claim 19 wherein said compound is an antisense sequence.

21. The method of claim 19 wherein said compound is an antibody specific against a diabetes-mediating protein antibody.

22. The method of claim 19, wherein said compound is a diabetes-mediating protein.

23. The method of claim 22, wherein said diabetes-mediating protein is selected from the group of proteins of Tables 1 and 2.

24. The method of claim 19, wherein said compound enhances or increases the expression of a diabetes-mediating protein.

25. The method of claim 19, wherein said compound inhibits or decreases the expression of a diabetes-mediating protein.

26. The method of claim 25, wherein said compound is a polynucleotide which inhibits the *in vivo* expression of a diabetes-mediating protein.

27. A method for identifying a compound capable of modulating the activity of a diabetes-mediating protein, comprising treating cells, tissues, or animals with a test compound suspected of being capable of modulating the activity of a diabetes-mediating protein, and determining the effect of said compound on the activity of one or more diabetes-mediating protein(s).

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